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Electroconvulsive Therapy in the Treatment of Mood Disorders: One-Year Follow-up

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ABSTRACT

Introduction: Electroconvulsive therapy (ECT) is known to be an effective option in the treatment of mood disorders, especially resistant depression. However, the remission achieved by ECT was reported to be not long lasting enough. The aim of the present study was to investigate the relapse/recurrence rates and associated risk factors during the first year after ECT in patients diagnosed with mood disorders.

Methods: In a naturalistic observation, patients diagnosed with unipolar depressive disorder or a depressive episode of bipolar disorder and who had achieved remission by ECT were followed up for at least one year. The patients were evaluated with structured interviews during the follow-up period. The relapse/recurrence rates were the primary outcome measurements, while hospitalization and suicide attempts were the secondary outcome measurements. The remitted and non-remitted patients were compared regarding the clinical features, ECT, and pharmacological variables.

Results: Fifty of 62 patients who had achieved remission with ECT completed the one year follow-up period. Thirty-three patients (66%) had relapse/recurrence, while 17 (34%) patients remained in remission. The relapse rates were similar in patients with unipolar depression and bipolar disorders. The mean number of ECT sessions was higher in relapsed patients with bipolar disorders. Multiple episodes were more frequent in non-remitted patients with unipolar depression. Comorbid psychiatric diagnosis was higher in non-remitted patients with unipolar and bipolar disorders.

Conclusion: The relapse/recurrence rate was found to be fairly high in the first year of follow-up in patients who had achieved remission with ECT. ECT decisions should be made carefully in patients with comorbid psychiatric diagnosis and multiple episodes as these are more risky. The ECT application procedure and successive maintenance treatment (maintenance ECT, pharmacotherapy, and psychotherapy) should be planned to sustain the remission for patients with mood disorders in long-term follow-up.

Keywords: Electroconvulsive therapy, mood disorders, relapse, remission, major depression

INTRODUCTON

The efficacy of pharmacotherapy in mood disorders is not satisfactory, and the desired remission rates are not currently achieved in either unipolar (UD) or bipolar disorders (BP) (1,2,3). Electroconvulsive therapy (ECT) has been used for a long time with successful response and remission rates; 80–90% of patients experience an improvement, and the efficacy of ECT has been established to be between 60% and 90% regarding acute response in treatment-resistant depression (3,4,5,6,7). ECT is also considered to be an effective treatment in bipolar depression and is indicated to be equally effective in unipolar and bipolar depression (8,9,10). The effectiveness of ECT in the treatment of UD and BP has also been reported, and it is recommended by guidelines (11,12,13,14). However, the literature data regarding the duration of remission achieved by ECT are limited and conflicting. Early studies reported that 50% of patients who responded to ECT relapsed within the first 3 months without any continuation therapy (15,16). To date, only a few controlled continuation studies have been published with short follow-up durations, such as six months (17,18). The few studies in the literature with longer durations but having a small number of patients, an uncertain definition of remission, or with a retrospective design were not informative (19,20).

Sacheim et al. (17) reported that 84% of their study patients with placebo relapsed in a 24-week trial. Even with continuation pharmacotherapy and/or the continuation of ECT, the relapse rate was reported to be between 40% and 50% within six months (17,21,22). In a meta-analysis, almost half of the patients relapsed in the first year of maintenance therapy and the majority relapsed in the first six months (23). Continuation pharmacotherapy was found to be more effective than a placebo in that study. However, the pharmacologic evidence was mostly provided by tricyclic antidepressants. The efficacy of newer antidepressants in the continuation period following ECT is not well documented.

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On the other hand, some regional or logistic factors, accessibility of ECT, mental health service quality, and indications of the ECT decision may affect the remission and relapse/recurrence rates. The aim of this study was to investigate the relapse rate of patients diagnosed with mood disorders who had achieved remission with ECT during the long-term follow-up. The secondary aim was to determine the clinical variables associated with the relapses.

METHODS

Subjects

The inpatients and outpatients diagnosed with unipolar depression or a depressive episode of bipolar disorder who had achieved remission with ECT for an index depressive episode were followed up at least one year using a naturalistic design. The patients were recruited from the ECT unit, and the diagnosis and comorbid diagnoses were verified using the Structured Clinical Interview for DSM-IV (SCID) (24,25). The Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) (26) was administered for the assessment of personality disorders. The primary physician of the patients managed the ECT decision and the pharmacological treatment plan in the acute treatment phase and continuation period. Three interviews (at baseline, 6 months, and 12 months) were done with the study patients: the diagnostic interviews were at baseline, the clinical data and relapse/recurrence and re-hospitalization were evaluated at 6 months, and the end of the study involved a structured interview. The caregivers/primary relatives were also interviewed for confirmation of the clinical outcome. The demographics, clinical data, severity of the symptoms, past history, comorbid medical or psychiatric problems, and functioning were provided from the hospital records retrospectively as confirmation of the interview; also, the reports of the primary physicians were reviewed during the follow-up period regularly. The patients were screened and included in the study between January 1, 2013, and August 30, 2014, and completed the follow-up period on August 30, 2015. The Ethical Committee of Istanbul University, Istanbul Medical Faculty, approved the study. The patients were informed about the study, and those who had given written consent were included in the study.

Inclusion criteria

1. Ages between 18 and 65 years old.
2. Diagnosis of MDE (single episode or recurrent) or MDE of BP (type I or II) by DSM-IV criteria.
3. Administration of ECT for a current index episode (with/without concomitant pharmacotherapy).
4. Achievement of remission with ECT for index episode.
5. Not having a medical illness with a causal relationship with MDE.

Outcome

The follow-up duration was initiated after the last ECT session with treatment of an index depressive episode. Remission is defined as a score of 7 or less on the 17-item Hamilton Depression Rating Scale (1). The primary outcome measure was the relapse/recurrence rate during the one-year follow-up period.

Relapse was defined as the return of the symptoms of depression before a full remission was reached within the first six months. Recurrence was defined as the appearance of another new episode of depression after full remission of a previous episode was achieved. We counted relapse and recurrence together. The hypomanic, manic, and mixed episodes according to DSM-IV criteria were also assessed as relapse in patients diagnosed with BP. The symptoms and the severity of the illness were evaluated with SCID-I. Suicidal ideation and re-hospitalization were designated as secondary outcome measures.

ECT and treatment parameters

ECT was applied in the ECT unit of the inpatient clinic by an ECT team to all of the patients with a standardized modality. The initial stimulus energy was determined by an age-based method adjusted for gender (27). The seizure details (current, pulse, seizure duration, anesthetic medications, dosage, etc.,) were recorded on the charts. The data related to ECT sessions and seizure were collected from these charts. ECT was delivered three times per week under monitored conditions. ECT was delivered with a Thymatron System IV Somatics LLC machine and brief pulse stimulator. This included a 4-channel digital EEG in order to measure the length and structure of seizures. The energy delivered was between 20 and 120%, while the charge delivered was between 108 and 648 mC. Propofol (0.5–1 mg/kg) was used as a short-acting anesthetic substance, and succinylcholine (1 mg/kg) was used as a muscle relaxant.

The electrodes were bitemporally placed. Seizures longer than 20 seconds in the EEG monitoring were accepted as therapeutic. The number of ECT sessions, concomitant medications during ECT, and pharmacological maintenance treatment during the follow-up were determined by the primary physician of the patients based on the clinical improvement needed to achieve remission. Concomitant antidepressant treatment was allowed during ECT.

Statistical analysis

All the statistical analyses, descriptive values, frequencies, percentages for categorical variables, mean, median, and SD values for the continuous variables were performed with the Statistical Package for the Social Sciences version 16.0 (SPSS Inc., Chicago, IL, USA).

The characteristics of the remitted and non-remitted patients were compared using t tests for the normally distributed continuous variables, Mann–Whitney tests for non-normally distributed continuous variables, and χ^2, Fisher exact χ^2 tests for the categorical variables. The level of statistical significance was determined at $p \leq 0.05$.

The patients having relapses/recurrences were recorded during the one-year follow-up and classified as non-remitted patients. The remaining patients who continued the remission and the non-remitted patients were compared with regard to the clinical variables in each of two different diagnoses (unipolar and bipolar disorder).

RESULTS

Patient characteristics

Sixty-two patients were eligible for the follow-up study. Nevertheless, only 50 of the 62 patients completed the study. The remaining patients were lost to follow-up owing to living in suburban areas, such that they did not continue their follow-up visits even though they accepted to participate. The diagnoses of the patients were as follows: 20 of 50 (40%) patients had bipolar depression, while 30 patients (60%) had UD.

Outcome measurements

Thirty-three (66%) of the 50 patients had relapse/recurrence during the one-year follow-up period. Sixteen of the 33 patients (48.5%) relapsed during the first six months, while 17 patients (51.5%) relapsed during the second six months of the follow-up period. Fourteen of 20 patients (70%) with BP and 19 of 30 patients (63.3%) with UD relapsed. The diagnostic groups were not different with regard to relapse rate (p=0.85).

The remitted and non-remitted patients were compared separately according to the diagnosis of BP or UD (Table 1). The mean relapse/recurrence time was 6.34 ($\pm$1.97) months for all patients, while the median was

Table 1. Clinical variables of the remitted and non-remitted patients

Diagnosis	UD (n=30)			BP (n=20)		
n (%)	Remitted patients 11(36.7)	Non-remitted patients 19(63.3)	p	Remitted patients 6(35)	Non-remitted patients 14(65)	p
Mean age (SD)	39.0 (7.64)	39.89 (10.83)	0.81	39.83 (8.27)	36.71 (10.50)	0.53
Female gender (%)	6 (54.5)	11 (57.9)	0.85	4 (66.7)	9 (64.3)	0.66
Family history for mood disorders (%)	5 (45.5)	10 (52.6)	0.70	2 (33.3)	5 (35.7)	0.66
Having multiple episodes (%)	3 (27.3)	14 (73.7)	0.02	3 (50)	11 (78.6)	0.3
GAF before ECT (SD)	19.72 (9.56)	21.84 (9.31)	0.55	22.66 (8.40)	19.14 (5.90)	0.29
GAF after ECT (SD)	56.36 (7.44)	57.89 (6.08)	0.54	60.00 (7.07)	53.25 (16.70)	0.35
Mean Number of ECT session (SD)	7.72 (2.83)	7.63 (2.83)	0.90	6.33 (2.42)	9.57 (2.95)	0.03
Mean duration of seizure, second (SD)	29.45 (10.27)	34.05 (14.69)	0.36	36.83 (11.05)	42.71 (15.48)	0.41
Having previous ECT (%)	4 (36.4)	6 (31.6)	0.54	1 (16.7)	6 (42.9)	0.27
Concomitant AD Treatment with ECT (%)	8 (72.7)	14 (73.7)	0.63	3 (50)	5 (35.7)	0.45
Maintenance AD (%)	9 (81.8)	14 (73.7)	0.48	3 (50)	5 (35.7)	0.45
SSRI/Other AD (%)	5/6 (45.5/54.5)	7/12 (36.8/63.2)	0.64	3/1 (75)	3/2 (60)	0.59
Maintenance SGA (%)	4 (36.4)	6 (31.6)	0.54	6 (100)	11 (78.6)	0.31
Maintenance MS (%)	1 (9.1)	5 (26.3)	0.26	6 (100)	8 (57.1)	0.07
Having psychotic symptoms (%)	2 (18.2)	6 (31.6)	0.36	2 (33.3)	6 (42.9)	0.54
+ suicide history at index episode (%)	3 (27.3)	6 (31.6)	0.57	0 (0)	2 (14.3)	0.47
+ previous suicide history (%)	3 (27.3)	10 (52.6)	0.16	0 (0)	3 (21.4)	0.52
Comorbid psychiatric diagnosis (%)	4 (36.4)	14 (73.7)	0.03	2 (0)	10 (71.4)	0.04
Comorbid personality disorder (%)	1 (9.1)	3 (47.4)	0.33	1 (16.7)	4 (35.7)	0.20
Suicide at follow-up (%)	0 (0)	9 (47.4)	0.004	0 (0)	8 (57.1)	0.008
Re-hospitalization at follow-up (%)	0 (0)	10 (52.6)	0.003	0 (0)	9 (64.3)	0.005

UD: unipolar depression; BP: bipolar disorder; AD: antidepressant; SGA: second generation antipsychotics; MS: mood stabilizer

7 (3–10) months. This was 6.05 (±1.80) months for UD and 6.76 (±2.20) months for BP. The UD and BP groups were not different regarding the duration of remission (MWU=96.500, p=0.305).

Nineteen (38%) of the 50 patients were re-hospitalized during the follow-up; all of them were in the non-remitted patients group. Seventeen patients (34%) (9 UD, 8 BP) had a suicide attempt during the follow-up period; one patient without any depressive relapse in the remitted group took an overdose of medication during an anger attack. She admitted herself to emergency and explained that it was a family conflict, and she did not have a suicide plan. This case was not considered as a relapse; thus, there was no depressive symptom. The remaining 16 patients were in a depressive relapse/recurrence and were re-hospitalized.

Clinical features

Five patients diagnosed with BP also had hypomanic/manic relapses. The ratio of patients with hypomanic/manic relapse among the patients with BP was 25%, and depressive relapses were seen in 11 patients (55%) with BP. The number of patients having any kind of relapse during the follow-up was 14 of 20 patients (70%) with BP and 19 of 30 (63.3%) patients with UD. The ratio of multiple episodes was significantly more frequent in non-remitted patients than in remitted patients with UD. Having multiple episodes as an independent variable seems to affect the relapses with an odds ratio (OR) of 7.467 [95% CI=1.40, 39.84; c2 (1, n=30)=6.111, p=0.02]. However, the number of patients was low and did not warrant further analysis. There was no such difference in patients with BP (78.6% vs. 50%, p=0.3).

The rate of concomitant antidepressant medication and maintenance pharmacotherapy are summarized in Table 1, and we did not find any difference on pharmacotherapy between the remitted and non-remitted patients of both the UD and BP patients. Non-remitted UD patients tended to have other types of antidepressants (SNRI and atypical antidepressants) than SSRIs.

Eleven (22%) patients had a history of one or more recent suicide attempts before ECT, but there was no relation between the prior suicide history and the relapse/recurrence rates (Table 1). Global Assessment of Functioning (GAF) was evaluated before and after ECT. There was no difference across the remitted and non-remitted patients for the values before and after ECT (Table 1). There was no difference between the remitted and non-remitted patients in terms of single or multiple episodes.

Thirty patients (60%) had comorbid psychiatric diagnosis, with the most common being as follows: 9 patients had personality disorders (5 borderline personality disorder, 3 obsessive compulsive personality disorder, 1 narcissistic personality disorder), 7 patients had anxiety disorders, 5 patients had posttraumatic stress disorder, and 4 patients had obsessive compulsive disorder. The ratio of patients with comorbid illness was significantly higher in the non-remitted groups of both the UD and BP groups (p=0.03 and p=0.04, respectively). The personality disorders were not different across the groups. We could not make a further analysis due to the limited patient numbers.

ECT treatment parameters

The mean number of ECT sessions was not different in the remitted (7.72±2.83) and non-remitted (7.63±2.83) groups of UD (p=0.90). However, the non-remitted patients of BP (9.57±2.95) had many more ECT sessions than the remitted patients (6.33±2.42) (p=0.03). The mean duration of ECT seizures was not different between the remitted and non-remitted patients of the UD and BP groups (p=0.36 and p=0.41, respectively). The mean postictal suppression index was 69.00% (±18.64) for the non-remitted patients and 73.27% (±19.28) for the remitted patients. Even though this EEG parameter tended to be higher in the remitted patients, it did not reach statistical significance (p=0.45).

DISCUSSION

In this study, the results showed that the duration of remission achieved by ECT was not long enough for patients with UD and BP in one-year follow-up. We found that only 34% of all patients sustained remission, which is a striking result. This high relapse rate is one of the highest rates in literature, which vary between 44.7 and 64.3% in patients with mood disorders (17,18,21,23,28). Prudic et al. (22) found disappointingly low remission rates with ECT in a community setting that are noteworthy to understand the real world, similar to our findings, but the follow-up duration was 6 months in their study. For a longer duration, excessive relapse rates might be expected. A meta-analysis found that 51.1% of patients relapsed in the first year after ECT and the highest relapses were seen in the first 6 months, similar to our results (23). The notable high relapse/recurrence rate of this study could be explained by several causes. First, the primary outcome measurement was relapse/recurrence rate and we defined the remission clearly. However, some studies in the literature counted the re-hospitalization, re-admission, and suicide attempt rates as an indicator of relapse, which are lower than the actual relapse rates (29). Moreover, re-hospitalization, re-admission, and suicide rates vary according to the conditions of the mental health services and are thus not a good indicator for relapse. We found less re-hospitalization and suicidal behaviors than relapse/recurrence rates, which supports this argument. Another issue, the quality of the mental health services for outpatients, may explain these high relapse rates. The number of patients lost to follow-up was not low in this study, and this may also indicate the poor quality of outpatient mental health services or patients' attitudes. Thus, intensive follow-up procedures should be institutionalized after ECT. The patients may seek psychiatric treatment for only severe episodes that require hospitalization in rural/provincial or suburban regions. They drop out from maintenance treatment and also might be non-adherent to pharmacotherapy after the acute treatment. The last but not least reason is the ECT decision of the physicians might need to be taken into consideration. The mental health policies, the expense of inpatient treatments, time restrictions, behavioral outbursts, suicidality, and expectations of patients/families for rapid cure may cause inappropriate ECT decisions.

This is the first study regarding the relapse rates of mood disorders treated with ECT and involving a follow-up study in Turkey. The regional literature data is very limited in ECT. In some retrospective chart reviews, ECT was administered to 2.2–16% of outpatients in all diagnostic groups (30,31,32). Cimilli et al. (33) reported that ECT was administered to 16% of BP patients in an inpatient unit in a retrospective study. Nevertheless, this involved a very small sample size, single site, and a retrospective study.

One of the two clinical features related to the higher relapse/recurrence for both UD and BP was comorbid illness. We found almost two times higher comorbid psychiatric illness in the non-remitted group. Our results indicated that the effectiveness of ECT in long-term follow-up is not high and that physicians should be aware of the longitudinal data with risky patients having multiple episodes before making the ECT decision. These results also highlight the importance of using guidelines and standard protocols for ECT in pre- and post-treatment phases. An interesting study came out recently showing a decline in the use of ECT (34). Despite there being several reasons for this decline, considering also the results of our study, high relapse rates might result in diminished ECT use in future.

The high comorbid psychiatric diagnosis associated with the high relapse/recurrence rate is consistent with the literature (35,36). Nordenskjöld et al. (37) found that substance abuse was a predictor of relapse/remission. In terms of cultural diversity, we did not find the substance abuse comorbidity as the most common one. Instead, comorbid anxiety disorders, namely PTSD and OCD and personality disorders, seem to be a risk factor for high relapse/recurrence rates in our study. Comorbidity needs special attention in the management of mood disorders, and it requires additional treatment modalities. However, there is little evidence about the effectiveness of ECT in patients with anxiety disorders (38,39,40). Moreover, there is evidence that high somatic anxiety and hypochondriasis predict a low likelihood of sustained remission with ECT (41). Untreated comorbid anxiety symptoms might be a predictor of relapses of mood disorders. Comorbidity of personality disorder was also reported to show less response to ECT (42). The results of this study revealed that comorbidity should be kept in mind as a remarkable risk factor for high relapse/recurrence rates. The second clinical difference between the remitted and non-remitted patients is the ratio of single to multiple episodes. We found that the patients with multiple episodes were less likely to have remission with ECT, which is in line with the literature (43). This is another important point when making ECT decision. This is another important point when making an ECT decision in the treatment of UD. The number of ECT sessions was higher in non-remitted patients with BP even though there was no difference for UD. Treatment resistance in bipolar depression might require a great number of ECT sessions and result in a shorter duration of remission. Even though an equal effectiveness of ECT was shown in patients with UD and BP, there could be some outcome differences (9).

The suicide and history of suicide attempts feature for the index episode were not different between the remitted and non-remitted patients. Suicidal thoughts/behaviors should be differentiated in the context of personality disorders and mood disorders. The presence of accompanying affective instability, impulsiveness, self-mutilating behaviors, and dysphoric mood states should be interpreted in the support of borderline personality disorder and a psychotherapeutic approach should be preferred first in these patients rather than ECT (39).

The depressive episodes with psychotic and non-psychotic features were not different with regard to relapse/recurrence in this study, whereas the patients with delusional depression who were treated with ECT showed a better response than those with non-delusional depression, despite the opposite findings in several reports (22,40). The concomitant medication use was not different between the remitted and non-remitted groups in this study. The variability of dosage, their impacts on seizure during ECT, and the details of subgroups of antidepressants were not assessed; hence the results are inconclusive for the effects of medication. However, it was recommended to continue medication, especially antidepressants and mood stabilizers, even in combination, to prevent recurrence in severely depressed inpatients in the literature (19). On the other hand, there are some reports that state that antipsychotics and benzodiazepine use were associated with an increased relapse rate (32). Even though there was no statistical difference, the remitted patients of BP tended to use more mood stabilizers. We did not find any difference for remission time and outcome in patients with BP and UD.

Even though we made comparisons with both unipolar and bipolar depression, there was no difference in the ratio of the illness type.

Even though ECT is an effective option for BP, it was reported that patients with UD respond better to ECT than do patients with BP (9,38). Our sample size may not differentiate the diagnostic effect on the relapse rate. There was no difference in the use of mood stabilizers, antidepressant treatment, and SGA across the study groups in regard to maintenance treatment, but these results might be related to the chronic and treatment-resistant course of both the BP and UD groups.

The continuation and maintenance of ECT is recommended as a valuable treatment modality to prevent the relapse and recurrence of mood disorders in patients who have responded to an index course of ECT (4). The American Psychiatric Association guidelines of ECT (11) advise the continuation of therapy with either pharmacotherapy or the continuation of ECT.

Study limitations

The main limitation of the study is its naturalistic design that yields less information in uncontrolled variables, especially in pharmacologic treatment. The various medications in this relatively small number study population do not allow conclusive analysis of their impacts on remission. The primary physicians determined the concomitant antidepressants to use during ECT and maintenance pharmacological treatment. Even though we obtained the data about the medications in the follow-up period, the different classes and dosage regimen of the different antidepressants could not be assessed. The results indicate that randomized controlled trials are needed to demonstrate the impacts of concomitant medications on the duration of remission. Some of the clinical data (illness history, clinical variables, etc.) were collected retrospectively. Even though the entire data source, i.e., the hospital records, were evaluated carefully, possible missing points are inevitable. Hence, we confirmed these data with two interviews during the follow-up. Nonetheless, the three follow-ups over one year duration might have provided limited information. Third, the non-standardized ECT procedure may create confounding effects. Although the variables related to ECT, such as electrical stimulus dosage and seizure duration, were applied in a consistent way, some parameters were missing in some seizures, such as the postictal suppression index. Therefore, we calculated the mean value of the postictal suppression index. The relatively small patient numbers might also explain the absence of significant differences between the remitted and non-remitted groups (i.e., lack of power). Therefore, we could not carry out further analyses of the statistically significant variables, such as having multiple episodes and comorbid diagnosis. Mood swings, elevations other than hypomania, mania, or major depression were not assessed with mood rating scales. Thus, only the clinically significant mood episodes meeting DSM-IV criteria were detected. Another limitation is that the subtypes of depression other than unipolar/bipolar and psychotic features were not evaluated in this study.

In conclusion, our study revealed that the one-year outcome in patients remitted with ECT was dramatically unsatisfactory. Consequently, ECT indications, the application procedure and successive treatment plan, and intensive follow-up should be structured carefully to improve the sustained remission. The comorbid psychiatric diagnoses and having multiple depressive episodes seem to be risk factors for relapse/recurrence and need special attention. Additional treatment modalities, such as psychotherapy, and continuation of ECT may be beneficial to sustain the remission and should be planned when making the ECT decision.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul University İstanbul School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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